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09/787,844	08/06/2001	Shujath M. Ali	DEX-0176	7509

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EXAMINER

YU, MISOOK

ART UNIT PAPER NUMBER

1642

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/787,844

Applicant(s)

ALI ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 12-21 is/are pending in the application.
- 4a) Of the above claim(s) 1-7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8,9 and 12-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Exhibits A, B, and C.</u>              |

### **DETAILED ACTION**

Applicant's Reply under 37 CFR § 1.111 filed on January 23, 2004 is acknowledged. The last Office action mailed on October 23, 2003 is rendered moot and replaced by this Action, because the Office action was based on examination of the invention not elected by applicant in the Election Paper filed on June 5, 2003, as applicant pointed out in the Reply. The error in the last Action is regretted. The corrective Action is as follows:

#### ***Election/Restrictions***

Applicant's election in the Paper filed on June 5, 2003 with traverse of group III, drawn to in vivo imaging using an antibody against a CSG wherein CSG comprises SEQ ID NO:1 is acknowledged. The traversal is on the ground(s) that the special technical feature linking claims 1-11 (since then, claims 10, and 11 have now been cancelled in the amendment filed on August 26, 2003) is the recognition that the CSG of SEQ ID NO:1 is a specific marker for gynecologic and testicular cancers. This is not found persuasive because: A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; (2) A product and a process of use of said product; (3) A product, a process specially adapted for the manufacture of the said product, and a use of said product; (4) A process and an apparatus or means specifically designed for

carrying out said process; or (5) A product, a process specially adapted for the manufacture of said product, and an apparatus or means specifically designed for carrying out said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).)

In the instance case, group I invention is drawn to method involving measuring SEQ ID NO:1 (nucleic acid), group II is drawn to antibody to SEQ ID NO:1 (nucleic acid), and group III (the elected group) is drawn to method involving a product that does not share a special technical feature with the products in claims that belong to group I, and II. In other words, the claims of the elected group III are drawn to method of using an antibody to a protein for in vivo imaging. Thus, the unity among claims that belong to group I, II or III, does not exist. The requirement is still deemed proper and is therefore made FINAL.

The original claim 8 that belongs to the elected invention was drawn to method using an antibody that binds SEQ ID NO:1 but the amended claim 8 is drawn to method using an antibody that binds to SEQ ID NO:2. The specification as originally filed at page 4, lines 23-30 discloses that SEQ ID NO:2 (CGS) disclosed in the instant application is used for imaging. CGS is used to designate both SEQ ID NO:1 (nucleic acid) and SEQ ID NO:2 (protein). The specification as originally filed at page 7, lines 1-

6, has a support for antibody against CGS or fragment. Thus, it is concluded that the invention claimed in amended claim 8, or the new claims 12-21, is not a new matter.

Claims 1-7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed on June 5, 2003.

Claims 8, 9 are amended, and claims 12-21 are new. Claims 1-9, and 12-21 are pending. Claims 8, 9, and 12-21 are examined on merits.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9, and 12-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The base claims 8, 14, and 18 recite "a Pro104 polypeptide" but it is not clear what the metes and bounds are. The specification at page 18, line 15, and page 25 lines 17 and 18 implies that "a Pro104 polypeptide" is either SEQ ID NO:2 or protein encoded by SEQ ID NO:1 with Clone ID 1450626 and Gene ID 236019. The specification at page 25 lines 17-32 appears to describe homology of SEQ ID NO:2 (Pro104) to other serine proteases. It appears that the specification limit "Pro104" to SEQ ID NO:2 or the protein encoded by SEQ ID NO:1 with Clone ID 1450626 and Gene ID 236019. The description of "Pro104" primary structure as compared to other serine

proteases at pages 25, lines 17-32 implies that Pro104 is SEQ ID NO:2. However, claims 8, and 13 as currently construed imply that "a Pro104 polypeptide" is a genus that SEQ ID NO:2 belongs to. Also note claim construction of claim 14 vs. claim 17, and claim 18 vs. claim 21.

Claims 8, 9, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: detection and determination steps to accomplish the purpose in the preamble of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 9, 12-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This written description rejection is made because the specification at page 7 lines 6-9 defines "antibody" to include "aptamers and single-stranded oligonucleotides". Therefore, claims 8, 9, 12, 13, 14-21 are interpreted as drawn to method using **a genus of "antibodies"** that specifically binds to

SEQ ID NO:2, wherein **said genus includes “aptamers and single-stranded oligonucleotides”**.

Voet et al., (1990, Biochemistry, John Wileys & Sons, page 1099 only) teach that an antibody has amino acids as its chemical structure. In other words, an antibody is a protein. Chaloin et al., (2002, Nucleic Acids Research, vol. 30, pages 4001-4008) teach at page 4001, left column, that aptamers are nucleic acid ligands that bind to target proteins. It appears that applicant acts as his/her own lexicographer because the art does not appear to define a nucleic acid molecule to be an “antibody”.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Probe Inc., 63 USPQ2d 1609; and Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is “what it does” as regard to “aptamers and single-stranded oligonucleotides”, species of “antibody” according to applicant’s own definition. The recitation “antibody” as understood by the art i.e. IgG, IgM, etc does not lack written description because the Board of Patent Appeals and Interferences has taken the position that once an antigen has been

isolated, the manufacture of antibodies against it is a routine matter in the current state of art. See *Ex parte Erlich* 22 USPQ2d 1463 (BdPatApp&Int 1992).

However, the specification lacks written description for “aptamers and single-stranded oligonucleoties” that specifically bind to instant SEQ ID NO:2. There is not even identification of any particular portion of a nucleic acid structure(s) that must be conserved in order to have the recited function i.e. “specifically binds to a Pro104”. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Chaloin et al., (cited above) teach that nucleic acid binding ligands to a specific protein has to be screened by SELEX procedure. See the heading “INTRODUCTION” at page 4001. This suggests that the chemical structure of “apatmers or single-stranded oligonucleotides” that specifically binds to instant SEQ ID NO:2 has to be screened. The specification does not teach a single “apatmer” structure that specifically binds to SEQ ID NO:2.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed nucleic acid structure(s) of the



“antibody” that specifically binds to SEQ ID NO: 2. Therefore, the art-defined antibody i.e. protein, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 8, 9, and 12-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

This rejection is based on the Office's interpretation of the nature of the invention as drawn to a method of imaging of a gynecologic cancer using an monoclonal or polyclonal antibody which specifically binds to SEQ ID NO:2 (claims 8, 12, 13), wherein said antibody is labeled (claim 9), or method of delivering a derivatized antibody (the specification at page 7 line 14, appears to limit “derivatized” as attaching cytotoxic agent or other art-known agents to an antibody that binds to SEQ ID NO:2), which specifically

binds to SEQ ID NO:2, to a gynecologic cancer cell in vivo (claims 14-17), or delivering said derivatized antibody to a gynecologic tumor in vivo (Claims 18-21). This rejection has several aspects.

First, the specification at page 4 lines 28-30 discloses that SEQ ID NO:2 is encoded by SEQ ID NO:1, which came from Incyte Pharmaceuticals, Palo Alto, CA according to the specification at page 16, first 3 lines under the heading "Example 1". Sequence search of instant SEQ ID NO:1 reveals that instant SEQ ID NO:1 is identical to a nucleic acid with ID AAX87151 disclosed in WO9936550-A2 (AE of IDS filed on 02/05/2002). Note Exhibit A. Also note the summary of ID AAX87151 at page 2, left column of Exhibit A, which states that the nucleic acid encodes HUPM-3 (see AAY06434). Also note that Incyte Pharm Inc., i.e. the source of instant SEQ ID NO:1, is the assignee of WO9936550-A2. AAY06434 of WO9936550-A2 is a 314 amino acids protein. Note Exhibit B. The different between AAY06434 and instant SEQ ID NO:2 is that instant SEQ ID NO:2 has extra 13 amino acids at the N-terminus starting with the first amino acid as Arginine (R). This indicates that either AAY06434 of WO9936550-A2 or instant SEQ ID NO:2 is an incorrectly annotated protein sequence because an identical cDNA sequence (i.e. instant SEQ ID NO:1 and AAX87151) encoding two different proteins (i.e. instant SEQ ID NO:2 and the protein of Incyte Pharm Inc. above) is logically implausible.

Search of instant SEQ ID NO:2 in SwissProt database indicates that five peer-reviewed journal articles have been published confirming presence of the protein sequence i.e. AAY06434 of WO9936550-A2 in a human genome. Note Exhibit C,

which shows that all of the human protein sequence deposited in the database confirm that the in vivo protein sequence lacks the first 13 amino acids of instant SEQ ID NO:2. Further, Darnell et al., (Molecular Cell Biology, Scientific American Books, 1990, page 442-3 only) teach that any in vivo translated protein has Met as the first amino acid. Instant SEQ ID NO:2 starts with Arg while AAY06434 of WO9936550-A2 starts with Met. The specification does not teach any evidence of in vivo expression of instant SEQ ID NO:2, while Hooper et al., (Cancer Research, 1999, vol. 59, pages 3199-3205) teach that a protein identical to AAY06434 is expressed in vivo (see page 3203). Thus, based on preponderance of evidence (that is the standard employed in the Office), it is concluded that that AAY06434 of WO9936550-A2 is a more likely correctly annotated protein sequence and instant SEQ ID NO:2 is a more likely incorrectly annotated sequence. It is concluded that it requires undue experimentation to practice the instantly claimed invention because it is seemingly impossible to use an antibody specifically binds to a protein (i.e. SEQ ID NO:2 ) that does not exist in vivo and/or is not expressed in vivo in first place.

The following enablement analysis is based the Office's interpretation that the instant SEQ ID NO:1 encodes the art-known protein, lacking the first 13 amino acids of instant SEQ ID NO:2.

The specification at Tables 1, and 2, page 24 discloses that the mRNA level corresponding to SEQ ID NO:1 is over-expressed in some ovarian cancer samples. However, the specification does not teach whether the corresponding protein is also over-expressed in ovarian cancer or any other gynecologic cancer. However, Hooper et

al., (cited above) teach at page 3204 that AAY06434 of WO9936550-A2 i.e. the protein corresponding to amino acid 14-327 of instant SEQ ID NO:2 is under-expressed in testicular cancer. The instant application appears to teach that over-expression of the gene product, the mRNA corresponding to SEQ ID NO:1, is correlated to ovarian cancer or testicular cancer. The instant application at page 8 lines 11-15, which speculates that detection of over-expression of the protein encoded by the disclosed nucleic acid molecule i.e. SEQ ID NO:1 in testicular cancer sample as compared to normal tissue samples could be a diagnostic assay. This indicates in order to use the instant claimed invention, one has to perform experimentation involving a large number of clinical samples from gynecologic cancers to determine whether the protein encoded by instant SEQ ID NO:1 is over-expressed because Hooper et al., (cited above) suggest that the protein encoded by instant SEQ ID NO:1 might be a tumor suppressor instead of a tumor antigen. Note the last line of abstract. It appears that Hooper et al., teach that under-expression of the protein is correlated with testicular cancer while instant specification appears to speculate over-expression of the protein is correlated with testicular cancer. This suggests that validation of the protein as a gynecologic cancer antigen is necessary in order to use the invention.

Tockman et al., (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer antigen to successful clinical application. Tockman et al., teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in

prospective population trials (see abstract). Early stage markers of tumorigenicity have clear biological plausibility as markers of preclinical cancer and if validated can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Although Tockman et al., are drawn to use of a cancer antigen for early lung cancer screening, the basic principles taught are clearly applicable to the instant invention because the specification has not established yet whether the protein encoded by instant SEQ ID NO:1 is a gynecologic cancer antigen that could be used as an in vivo imaging target. One of skill in the art would have to do undue experimentation to use an antibody that specifically binds to a protein encoded by SEQ ID NO:1 for in vivo gynecologic cancer imaging, given that the specification does not even teach whether said protein is a cancer antigen for a gynecologic cancer.

The specification does not disclose if the protein over-expression is correlated with any gynecologic cancer although the specification at Tables 1, and 2, page 24 discloses that the mRNA level corresponding to SEQ ID NO:1 is over-expressed in some ovarian cancer samples. The art recognizes that expression of mRNA does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al., (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide are translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al., (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not solely contingent on mRNA

expression due to the multitude of homeostatic factors affecting transcription and translation.

Further, the art recognizes that *in vivo* imaging using a labeled antibody, or delivering a derivatized antibody to gynecologic cancer cells or gynecologic tumors is not a trivial matter. Aloj et al., (2002, Biopolymers. Vol. 66, pages 370-80) teach that in order to target specific molecules inside the body using radiopharmaceuticals such as a radioisotope-labeled antibody, several parameters have to be considered: (1) the target protein should be over-expressed in cancer to be imaged; (2) a radiopharmaceutical should be tested to see whether said radiopharmaceutical specifically binds to the *in vivo* target *in vivo*; (3) how the unbound radiopharmaceutical is cleared for minimizing unwanted high background (note the abstract, and pages 372-373). The instant specification has failed to teach with a reasonable certainty that the protein encoded by SEQ ID NO:1 is a gynecologic cancer antigen while the art (see Hooper et al., above) suggests that the protein encoded by SEQ ID NO:1 is a tumor suppressor. Low et al., (1995, Radiology, vol. 195, pages 391-400) also teach that in order to image an ovarian cancer (a species of a gynecologic cancer), selection of an antibody that specially binds to an ovarian cancer-associated antigen, is the first necessary step (see page 391 middle column; the authors selected an antibody targeting Tag-72, a previously known ovarian cancer antigen). Low et al., further teach accuracy of imaging using an antibody directed to a cancer antigen has to be evaluated against other known cancer detection methods such as histology or pathology (note page 393 under the heading "Pathologic Proof", and Table 3 at page 396) Likewise, Krag et al., (1993, Arch. Surg.

Vol. 128, pages 819-23) teach method of imaging an ovarian cancer using a radio-labeled (i.e. indium 111-labeled) CYT-103 monoclonal antibody requires selection of an antibody capable of binding to an antigen that is over-expressed in an ovarian cancer (see page 820 under the heading "Patients, Materials, and Methods").

The instant application fails to teach whether SEQ ID NO:2 or a protein encoded by SEQ ID NO:1 is over-expressed in any gynecologic cancer, thus failing at the first required step leading to method of imaging a gynecologic cancer or delivering a derivatized antibody to gynecologic tumors or cancers. Further, the specification does not teach how to make "aptamers" that specifically bind to instant SEQ ID NO:2 or a protein encoded by instant SEQ ID NO:1, other than saying a screening technique called SELEX is known in the art. Note the written description rejection above for further details on this matter. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-



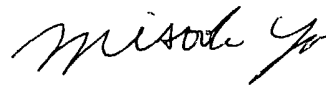
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272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.  
Examiner  
Art Unit 1642

A handwritten signature in black ink, appearing to read "Misook Yu", with a stylized flourish at the end.